

132. (New) The isolated protein of claim 123 wherein the amino acid sequence further comprises a heterologous polypeptide.

133. (New) The protein of claim 123, wherein said isolated protein is glycosylated.

134. (New) The protein of claim 123, wherein said isolated protein is pegylated.

135. (New) A composition comprising the isolated protein of claim 123.

136. (New) A protein produced by a method comprising:

(a) culturing a host cell under conditions suitable to produce the isolated protein of claim 123; and

(b) recovering the protein.--

Remarks

New claims 90-136 will be pending in the captioned application upon entry of the present response and amendment. The previously pending claims have been canceled and new claims 90-136 have been added to more particularly point out and distinctly claim the subject matter Applicants regard as the invention. The specification has been amended to correct an obvious typographical error. Support for new claims 90-136 is found in the claims as originally filed and throughout the specification.

In particular, support for new claims 90 and 96-100 is found, for example, at page 4, first full paragraph through page 5, first full paragraph; and at page 8, first and second full paragraphs. Support for new claims 106-107 is found, for example, at page 7, first and second full paragraphs. Support for new claims 113-117 and 123-131 is found, for example, at the paragraph bridging pages 6 and 7; and at page 7, second full paragraph. Support for

new claims 91-93, 95, 101-103, 105, 108-110, 112, 118-120, 122, 132-134, and 136 is found, for example, at the paragraph bridging pages 8 and 9; at page 12, second full paragraph; at page 13, first full paragraph; and at page 15, second full paragraph. Support for new claims 94, 104, 111, 121, and 135 is found, for example, at the paragraph bridging pages 16 and 17.

Thus, no new matter has been introduced.

I. Rejections of the Claims under 35 U.S.C. §112, First Paragraph.

The Examiner rejected claims 57-61, 71, 74, and 89 under 35 U.S.C. § 112, first paragraph. *See*, Paper No. 16, Pages 3-6. Applicants respectfully point out that the rejected claims have been canceled herein and therefore address the rejection as it applies to new claims 90-136. The Examiner rejected the claims under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In particular, the Examiner contends that "... the structural similarity between EMAP II and EMAP III cannot lead the skilled artisan to infer a functional similarity in the absence of supporting evidence." *See*, Paper No. 16, Page 5.

Applicants respectfully disagree and traverse.

A patent Applicant's specification that contains a teaching of how to make and use the invention must be taken as enabling unless the Patent Office provides sufficient reason to doubt the accuracy of the disclosure. *See, In re Marzocchi*, 439 F.2d. 220, 223-224, 169 U.S.P.Q. 367, 369-370 (C.C.P.A. 1971). The initial burden is on the Examiner to provide evidence why the skilled artisan would not be enabled to practice the claimed invention throughout the entire scope of the claims. *See, In re Wands*, 858 F.2d 731, 8 U.S.P.Q. 1400 (Fed. Cir. 1988). Applicants submit that the Examiner has provided no reasonable basis to doubt the objective truth or accuracy of the disclosure and has failed to support her allegations with evidence to

doubt the enablement of the claimed protein sequences. The Examiner notes that she finds no correlation between percent identity and function in only a few cases of proteins that are completely unrelated to the claimed polypeptides. Moreover, the Examiner provides no reasoning as to why the claimed polypeptides could not have any of the utilities asserted by Applicants. Accordingly, the Examiner has not met her burden in explaining why the skilled artisan would not be enabled to practice the claimed invention throughout the entire scope of the claims and the rejection based on this improper analysis should be withdrawn.

Applicants' original specification disclosed sequence identity between EMAP III and EMAP II. *See, e.g.*, specification at page 2, lines 13-15, at page 4, lines 15-17, and at Figure 2. EMAP II was shown by Kao, *et al.*, (*J. Biol. Chem.* 269:25106-19 (1994)) to activate endothelial cells, elevate cytosolic free calcium concentration, release von Willebrand factor, induce tissue factor, and stimulate expression of the adhesion molecules E-selectin and P-selectin. Moreover, neutrophils exposed to EMAP II protein demonstrated elevated cytosolic free calcium concentration, peroxidase generation, and chemotaxis. The EMAP II polypeptide also activated mononuclear phagocytes and elevated cytosolic free calcium concentration. A single intra-tumor injection of EMAP II into Meth A sarcomas induced acute thrombohemorrhage and partial tumor regression.

The specification also teaches that EMAP III (as shown in SEQ ID NO:2) is about 60% identical and about 75% similar to the active domain of EMAP II over 150 amino acids of the 168 amino acid sequence shown as SEQ ID NO:2. *See, e.g.*, Figure 2 of the application as originally filed. The Examiner contends that the structural similarity between EMAP II and EMAP III cannot lead the skilled artisan to infer a functional similarity in the absence of supporting evidence. In this regard, the Examiner cites several examples of molecules completely unrelated to EMAP III that are highly structurally similar to one another and exhibit divergent functions, but are completely unrelated to the claimed polypeptides. Applicants submit that the use of structure-function relationships between closely related proteins that are unrelated to the claimed polypeptides is an insufficient basis from which to evaluate the claimed polypeptides.

Because the Examiner has not provided a relevant basis for rejection, Applicants again assert the disclosed utilities for the claimed polypeptides and contend that one of skill in the art would immediately know how to make and use the claimed invention. Accordingly, Applicants respectfully assert that the rejection under 35 U.S.C. § 112, first paragraph, has been obviated and respectfully request that the rejection be withdrawn.

II. Rejection of the Claims under 35 U.S.C. § 102.

The Examiner has rejected claim 89 under 35 U.S.C. § 102(b) as allegedly being anticipated by WO92/15323 (Creative Biomolecules). *See*, Paper No. 16, Page 7.

Applicants respectfully disagree. However, solely in the interest of facilitating prosecution, Applicants have canceled claim 89. None of new claims 90-136 recite language analogous to the allegedly offensive language of now-canceled claim 89. Accordingly, the rejection under 35 U.S.C. § 102(b) has been obviated, and should therefore be withdrawn.

Conclusion

Entry of the above amendment is therefore respectfully solicited. In view of the foregoing remarks, Applicants believe that this application is now in condition for allowance. An early notice to that effect is urged. The Examiner is invited to call the undersigned at the phone number provided below if any further action by Applicants would expedite the examination of this application.

Finally, if there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

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Enclosures
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